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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/775,869	02/10/2004	Ekaterina Dadachova	96700/845	1864

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EXAMINER	
FETTEROLF, BRANDON J	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 09/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/775,869	DADACHOVA ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-19,25-33,35-37 and 41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 5-19, 25-33, 35-37 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Response to the Amendment

The Amendment filed on 06/27/2006 in response to the previous Non-Final Office Action (02/28/2006) is acknowledged and has been entered.

Claims 1-2, 5-19, 25-33, 35-37 and 41 are currently pending and under consideration.

Rejections Maintained:

Claims 1-2, 5-19, 25-33, 35-37 remain rejection and new claim 41 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating and/or imaging melanin containing melanoma in a subject comprising administering an amount of a radiolabeled antimelanin antibody, wherein the antimelanin antibody is 6D2, does not reasonably provide enablement for a method of treating and/or imaging any and/or all tumors, including melanoma, comprising administering any and/or all radiolabeled antibodies specific for melanin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 1-2 read on a method of treating and/or imaging a melanin containing tumor comprising administering a radiolabeled antibody which binds to melanin. Thus, claims 1-4 read a

method of treating and/or imaging any and/or all melanin containing tumors comprising administering any and/or all radiolabeled monoclonal or polyclonal antibodies specific for melanin. Claims 5-19, 25-33 and 35-37 read on a method of treating and/or imaging a melanin-containing melanoma comprising administering a radiolabeled antimelanin monoclonal antibody. Thus, the claims read on administration of any and/or all radiolabeled antimelanin antibodies.

The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art. The instant specification is not enabling for claims drawn to a method of treating and/or imaging any and/or all melanin containing tumors, including melanoma comprising administering any and/or all radiolabeled antibodies specific for melanin. The specification teaches (page 5, paragraph 0024) that the present invention involves a method of treating and/or imaging tumors in a subject comprising administering a radiolabeled antibody effective to treat or image the tumor, wherein the antibody binds to a cellular component released by a dying tumor cell including, but not limited to, a histone, a mitochondrial protein, a cytoplasmic protein or a pigment, e.g., melanin. With regards to the tumor, the specification teaches (page 6, paragraph 0030) that the term "tumor" includes melanoma. The specification further provides (page 13, paragraph 0055 to 0056 and page 14, paragraph 0059 to 0060) the in vivo binding/distribution of radiolabeled antimelanin antibody 6D2 in melanoma containing mice, as well as the radioimmunotherapy of melanomas using the radiolabeled antimelanin antibody 6D2. Moreover, the specification provides a prospective example (beginning on page 16, paragraph 0067) on how to make and/or use antibodies to human melanin. Thus, while the specification clearly conveys the treatment and/or imaging of melanin containing melanoma's comprising administering radiolabeled 6D2 anti-melanin antibody, the specification appears to be silent on the treatment of any other tumor or the specificity of any other anti-melanin antibody.

The closest prior art to the instantly claimed invention is Mason et al. (Cancer Research 1954; 14; 648-650), whom teaches a radiolabeled anti-melanin antibody (abstract). Specifically, the reference teaches that that administration of a radiolabeled anti-melanin antibody to mice bearing melanin containing melanoma's resulted in no significant localization of radioactivity, wherein the failure to localize may be ascribed to several causes, most likely of which is the relative

impermeability of mouse melanoma cells to rabbit antibodies (page 650, 1st column, 1st paragraph to 2nd paragraph).

As such, the instant specification provides insufficient guidance and objective evidence to predictably enable one of skill in the art to use the invention as claimed. Those of skill in the art would recognize the unpredictability of using any radiolabeled antibody to melanin for radioimmunotherapy and/or radio imaging. For example, Wilder et al. (J. Clin. Oncol. 1996; 14: 1383-1400) discloses challenges that currently face radioimmunotherapy (abstract). These challenges include: (1) circulating free antigen, biding of antibodies to nonspecific Fc receptors, insufficient tumor penetration, antigenic heterogeneity and insufficient antigen expression, antigenic modulation and development of human antimouse antibodies. Wilder et al. further teach the importance of dosimetry for treatment planning and assessment of results, wherein dosimetry is dependent on the kinetics of uptake and clearance of radiolabeled antibodies, the distribution of radiolabeled antibodies and the radioisotope attached to the antibody (page 1387, 1st column, 3rd paragraph from bottom). For example, Wilder et al. teach that the transport of antibodies through the intestinal space of a tumor by diffusion and convection is impeded by antigen binding and relatively large extravascular distances which results in a heterogeneous distribution of antibodies. Along the same lines, Erdi et al. (Phys. Med. Biol. 1996; 41: 2009-20026) disclose that although RIT (radioimmunotherapy) is an innovative and promising approach, there is problems to be solved which limit its use (page 2009, Introduction). These problems include: (1) the low uptake of the radiolabeled antibody; (2) the low target:non-target ratios and the inhomogenous distribution of antibodies within the tumor. While these reference demonstrate the importance of the specificity, uptake and distribution of the antibody in radioimmunotherapy, the same consideration and/or problems associated with RIT are found with radio imaging as well, see for example Chatel et al. (Eur. J. Nucl. Med. 1992; 19: 205-213). As such, in view of the teachings of Mason et al, supra, the skilled artisan would not have found sufficient guidance in the specification to achieve an effective method of treating an/or imaging tumors comprising administering any and/or all radiolabeled antibodies to melanin.

In view of the lack of guidance and the large amount of experimentation in an unpredictable art, it would require undue experimentation to practice the claimed invention.

In response to this rejection, Applicants assert that the teachings of Mason et al. reflect the technology of a half a century ago and not the state of the art readily available to the skilled artisan at the time the subject application was filed. First, Applicants assert that Mason et al. did not use a monoclonal antibody (this technology was first described in 1975), but only anti-melanin gamma globulin from sear, wherein the amount of melanin-specific antibodies is only a small fraction of the total immunoglobulin pool. Second, Applicants assert that Mason et al. used an outdated radiolabeling technique that resulted in extremely low specific activity of the radiolabeled antibody, i.e., 10 mCi/0.75 mg protein (~13 mCi/mg protein). In comparison, Applicants assert that much higher specific activities are routinely achievable with modern radiolabeling techniques as taught by Dadachova et al. PNAS 101: 14865-70, 2004). As a result of the extremely low specific activity of their labeled globulin, Applicants assert that Mason et al. effectively saturated all possible binding sites on extracellular melanin in the tumor with an enormous excess of unlabeled globulin. Hence, Applicants assert that the methodological limitations of low activity in labeling combined with only a minute amount of specific antibody can easily explain the inability of Mason et al. to obtain significant localization of radioactivity at the melanoma.

These arguments have been carefully considered, but are not found persuasive.

In response to Applicants assertion that Mason et al. does not represent the state of the art at the time the application was filed, the Examiner acknowledges and agrees with Applicants with respect to Mason not representing the state of the art at the time the application was filed. However, the Examiner recognizes that Mason et al. was incorporated into the body of the rejection as the closest prior art and not the state of the prior art. Therefore, Applicants arguments with respect to Mason et al. not reflecting the state of the art at the time the invention was filed do not appear to be relevant. In the instant case, Applicants do not appear to argue the unpredictability of using any radiolabeled antibody to melanin for radioimmunotherapy and/or radio imaging in view of the teachings of Wilder et al., Erdi et al. and Chatel et al., above. As such, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as written.

Therefore, NO claim is allowed

All other rejections and/or objections are withdrawn in view of applicant's amendments and arguments there to.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Patent Examiner
Art Unit 1642

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER

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